

Table showing the comparative Weight of Shells of similar Size.

Locality.	Level.	Extremes of length in mm.	Average length of 20 specimens.	Total weight in grams of 20 specimens.
Shore of Aral Sea	21—17	19·2	13·3
Shumish Kul	1st terrace	21—17	19·1	14·1
Ditto	2nd terrace	21—17	19·4	14·5
Ditto	4th terrace	21—17	19·2	6·5
Ditto	5th terrace	21—17	18·9	6·1
Ditto	7th terrace	21—17	19·7	4·6
Shore of Abu Kir	21—17	19·0	6·4
Jaksi Klich	Upper deposit	23—19	20·4	7·8
Ditto	Lower deposit	23—19	20·4	5·5
Jaman Klich	Lower deposit	21—17	19·2	5·1
Sub-fossil shells at Mandara	26—21	23·4	24·2
Shore of Mareotis	25—22	23·8	12·0
Ramleh Lake No. 1	(Fresh water)	25—20	21·4	18·3
Ramleh Lake No. 2	(Fresh water)	26—23	24·1	23·6

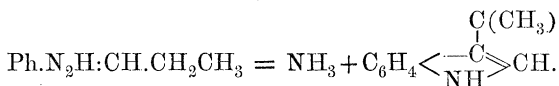
IV. "On the Occurrence of Skatole in the Vegetable Kingdom."

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Skatole is the name given by Brieger ('Deutsch. Chem. Gesell. Ber.,' vol. 10, p. 1027; 'Journ. für Prakt. Chem.' [2], vol. 17, p. 129) to a substance he obtained in 1887 from human excrement (τὸ σκῆρ, σκατός) which possessed the disgusting odour of the fæces. Nencki ('Journ. für Prakt. Chem.' [2], vol. 17, p. 98) soon afterwards recognised the same substance among the products of the decomposition of albumen by fused potash. Secretan ('Deutsch. Chem. Gesell. Ber.,' vol. 10, p. 1031) isolated skatole from the products of the putrefaction of albumen. Later, Salkowski ('Deutsch. Chem. Gesell. Ber.,' vol. 12, p. 651) separated it from the putrefaction products of flesh and afterwards from those of various forms of animal proteid ('Zeits. für Physiol. Chem.,' vol. 8, p. 417). Tappenheimer ('Deutsch. Chem. Gesell. Ber.,' vol. 14, p. 2382) has found skatole in the intestines of several herbivorous animals, and recently Stoeckh ('Deutsch. Chem. Gesell. Ber.,' vol. 20, p. 1108) has obtained it, along with indole and other substances, by distilling strychnine

with lime. Nencki ('Journ. für Prakt. Chem.,' vol. 20, 1879, p. 466) by a series of analyses of skatole and its picrate, showed that the composition of the substance is expressed by the formula C_9H_9N , and that it might be regarded as the methyl-derivative of indole (C_8H_7N), a compound which is associated with skatole in the fæces, and which is also produced during the putrefaction of albumen. In 1880 von Baeyer ('Deutsch. Chem. Gesell. Ber.,' vol. 13, p. 2340) described a method of preparing skatole, together with indole, from indigo, which was reduced with tin and hydrochloric acid, and the resulting reduction product distilled with powdered zinc. Three years later, in 1883, Otto Fischer and German achieved a synthesis of skatole ('Deutsch. Chem. Gesell. Ber.,' vol. 16, p. 710) by heating glycerol with a compound of zinc chloride and aniline, $C_6H_7N + C_3H_8O_3 = C_9H_9N + H_2O$. Fileti ('Gazz. Chim. Ital.,' vol. 13, p. 350) in the same year prepared skatole by distilling the barium salt of orthonitrocinamic acid with powdered zinc, $C_9H_{11}NO_4 + 3Zn = 3ZnO + H_2O + C_9H_9N$, and he inferred from this synthesis that skatole is Pr-3 methyl indole, an inference which has since been fully substantiated.

Quite recently a most interesting synthesis of skatole has been made by Emil Fischer ('Liebig's Annalen,' vol. 236, 1886, p. 137) from propylidene phenylhydrazide. This compound when heated with zinc chloride yields ammonia and Pr-3 methyl indole (skatole),



Neither skatole nor indole has hitherto been observed to occur in plants. They have appeared to be characteristic products of the bacterial resolution of animal proteid.

Among the many plants collected by the late Daniel Hanbury, F.R.S., and now deposited in the Museum of the Pharmaceutical Society, there was a small specimen of wood to which the Curator, Mr. E. M. Holmes, drew my attention on account of its intense odour, which recalled that of α -naphthylamine. Since α -naphthylamine has not been noticed as a plant constituent I determined to examine the specimen, which was labelled *Celtis reticulosa*, Java. It was evidently the wood of a large tropical tree.

In order to be well assured of the identity of the specimen I applied to Mr. Thiselton Dyer for information about this plant, and I am greatly indebted to him for the trouble he has taken in ascertaining what is known on the subject. Mr. Dyer informs me that "*Celtis reticulosa* was the name given by Miquel to a tree growing in Java. Planchon subsequently identified the species with *Celtis cinnamomea* of Lindley (De Candolle's 'Prodromus,' vol. 17, p. 181), which occurs throughout Eastern India and Ceylon. Thwaites regards the Ceylon

form as a distinct species, under the name of *Celtis dysodæylon* ('Enum. of Ceylon Plants,' p. 267). But botanists generally sink it with the Java species in *Celtis cinnamomea*. Thwaites says: 'The freshly cut timber of the tree possesses a powerful and very disgusting odour.' I have not come across any other notices of this singular property. But the evidence, though indirect, goes to show that your wood is correctly named and what it professes to be. *Celtis* belongs to the *Urticaceæ*."

The total quantity of the wood I was able to obtain amounted to rather less than 200 grams.

A small quantity of the finely powdered wood was moistened with water and distilled with steam. The first fractions of the distillate contained white particles which dissolved in the larger quantity of water that was subsequently condensed. The distillate was examined for naphthylamine, but none could be detected.

On submitting to steam distillation a larger quantity of the powdered wood, and extracting the aqueous distillate with light petroleum, a substance possessing an intolerable odour of fæces was obtained. It crystallised from water in colourless scaly crystals, which were dissolved by ether, alcohol, and benzene. The aqueous solution was not precipitated by a saturated solution of picric acid until the liquid had been strongly acidified with hydrochloric acid, when a dark red precipitate appeared. The dilute aqueous solution was not coloured or otherwise affected by the addition of fuming nitric acid or by a mixture of sodium nitrite and sulphuric acid, neither did it colour a pine shaving moistened with hydrochloric acid. By warming with hydrochloric acid the aqueous solution was coloured cherry-red. By these reactions the absence of indole was conclusively proved, but it seemed probable that the substance might be an indole-derivative.

The picrate was obtained by precipitating the aqueous solution (prepared from the ethereal extract of the distillate) strongly acidified with hydrochloric acid, with a saturated solution of picric acid. The dark-red precipitate was collected and distilled with dilute ammonia. The recovered substance was again converted into the picrate by a repetition of the process described above, and this was collected, washed with cold water, and dried over sulphuric acid. The dark-red needles of the picrate melted with some decomposition between 159—161° C. In a portion of this salt the nitrogen was determined by Dumas' method, the gas being collected through the limb of a Sprengel pump. [Weight of picrate taken 0.0258 gram; corrected volume of nitrogen obtained 3.2 c.c. Percentage of nitrogen in the picrate 15.5. Calculated for $C_9H_9N.C_6H_2(NO_2)_3OH$, 15.5 per cent. of nitrogen.]

It was thus proved that the substance possesses the composition of

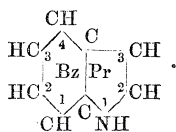
methyl indole. It remained to determine whether it corresponded with any of the known isomeric methyl indoles. These are Pr-1 methyl indole, which is liquid above $-20^{\circ}\text{C}.$; Pr-2 methyl indole (methyl ketole), which melts at $59^{\circ}\text{C}.$; Pr-3 methyl indole (skatole), which melts at $93-94^{\circ}\text{C}.$ (Nencki), $95^{\circ}\text{C}.$ (E. Fischer), and Bz-3 methyl indole, which melts at $58^{\circ}\text{C}.$ *

A crystalline specimen of the methyl indole was prepared from the picrate by distilling it with dilute ammonia. The distillate was extracted with ether, and the residue left by the evaporation of the ethereal solution was crystallised from water. These crystals were observed to melt at $93.5^{\circ}\text{C}.$, and were, therefore, identical with Pr-3 methyl indole, the skatole of Brieger. To completely confirm this conclusion a synthesis of skatole was made from propylidene-phenylhydrazide, and the properties of the synthetical skatole were found to be identical with those of the skatole from *Celtis reticulosa*. It was not possible with so small a quantity of material to estimate the amount of skatole contained in the wood, but it is extremely small, and is certainly considerably less than 1 per cent.

Conflicting statements exist with reference to the odour of skatole. The skatole from *Celtis reticulosa* undoubtedly possesses a strong faecal smell. Von Baeyer has stated that when pure, skatole has no faecal odour, while Brieger, Emil Fischer, and others assert that it has. Some curious facts were observed during the course of this investigation which may throw some light on the cause of this divergence of opinion. It was noticed that the faecal smell is most marked when the substance is present in minute quantities. When larger quantities of the substance are smelt the odour appears to be penetrating, but more aromatic than faecal. It also seems that after repeatedly smelling the substance the nose becomes insensitive to the effect of minute quantities and fails to recognize the faecal odour.

It may be useful to refer here to the delicacy of the various reactions for skatole and indole, since it is often important to recognise the presence of very small quantities of these substances in pathological fluids. The formation of the white insoluble nitroso-derivative from skatole by the action of nitrous acid cannot be

* The nomenclature followed is that proposed by Emil Fischer, the isomerides in which the substitution occurs in the pyrrole nucleus of indole being distinguished as Pr-derivatives, and those in which substitution takes place in the benzene nucleus as Bz-derivatives. The hydrogen atoms of the two nuclei are numbered in accordance with the following plan—



recognised in very dilute solutions, but the production, under the same conditions, of a reddish colour or precipitate is a sensitive test for the presence of indole.

By far the most delicate reaction for skatole consists in the development of a cherry-red colour when an aqueous solution is warmed with a few drops of strong hydrochloric acid. This reaction has been obtained with very dilute solutions. In moderately dilute solutions, strongly acidified with hydrochloric acid, a saturated solution of picric acid produces a red precipitate of skatole picrate.

The occurrence of skatole in the vegetable kingdom is of especial interest, and it is remarkable that the substance should make its appearance, or, at any rate, that it should accumulate, at a late period in the growth of the tree. The absence of indole is also significant. Sometimes skatole, without indole, is observed to result from the putrefaction of animal proteid, but usually both indole and skatole are formed. The occasional absence of indole, as well as the inconstancy of the relation between the quantities of indole and skatole formed during proteid putrefaction, has led Salkowski ('Zeits. für Physiol. Chem.,' vol. 8, p. 417) to regard the formation of each of these substances as due to the intervention of a special ferment, which he has called the indole ferment and the skatole ferment respectively. It must be remembered, however, that indole is less stable than skatole, and would be less likely to survive the effect of the various chemical changes which are proceeding during the later stages of putrefaction. Hoppe-Seyler ('Zeits. für Physiol. Chem.,' vol. 8, p. 214) has shown that if oxygen is freely supplied to a liquid in which proteid putrefaction is taking place, neither indole nor skatole is formed. The superior stability of skatole may possibly explain its survival in the plant. It would be interesting to determine whether indole is present in *Celtis reticulosa* at an earlier stage of its growth, as, for example, at the period when the skatole first makes its appearance.

It would also be of the highest biological and chemical interest to discover if possible the exact source of the skatole in this plant, to determine whether the vegetable proteid of *Celtis reticulosa* can be made to yield skatole by the methods which are known to lead to its production from animal proteid, or whether the skatole has been formed from some intermediate substance, as, for example, an amidated organic acid. The synthetical production of skatole from nitrocumic acid furnishes us with a clue to one possible mode of formation in the plant.

This investigation has been conducted in the Research Laboratory of the Pharmaceutical Society, and my thanks are due to Mr. W. A. Salter for the assistance he has given me with some of the experiments which are recorded in this paper.